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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,888	FEYT ET AL.	
	Examiner	Art Unit	
	OLUWATOSIN OGUNBIYI	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32,35-38,40,43-45,47 and 48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32,35-38,40,43-45,47 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/29/08 has been entered.

Claims 33-34, 39, 41-42, 46 have been cancelled. Claims 32, 35-38, 40, 43-45 and 47-48 are pending and are under examination.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

See p. 12 lines 9, 11, 17, 30; p. 14 line 5 and p. 16 lines 25 and 32.

Double Patenting

Applicant is advised that should claim 35 be found allowable, claim 48 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Both claims 35 and 48 recite:

A method of inducing an immune response against an inflection caused by *Neisseria meningitidis* or *Neisseria gonorrhoeae* bacteria in a human in need thereof, comprising administering to the human an effective amount of a pharmaceutical composition comprising a recombinant protein and a pharmaceutically acceptable carrier, wherein the protein comprises an amino acid sequence set forth in SEQ ID NO: 4.

Rejections Withdrawn

The rejection of claims 32 and 35-45 under 35 U.S.C. 112, first paragraph is withdrawn in view of the amendment to the claims.

The rejection of claims 33-34, 39, and 42 under 35 U.S.C. 102(b) as being anticipated by Fraser et al. WO 99/57280, November 1999 is withdrawn.

The rejection of claims 33-34, 39, and 42 under 35 U.S.C. 103 as being unpatentable over Fraser et al. WO 99/57280, November 1999 in view of Tai et al (WO 97/28273) Aug. 1997 is withdrawn.

The rejection of claims 32-36 and 39-45 under 35 U.S.C. 103 (a) as being unpatentable over Fraser et al. WO 99/57280, November 1999 in view of Meinke et al, WO 02/059148, Aug. 1 2002 is withdrawn in view of the cancellation of claim 41.

Rejections Maintained

The rejection of claims 32, 35, 36, 40, 43-45 and new claim 48 under 35 U.S.C. 102(b) as being anticipated by Fraser et al. WO 99/57280, November 1999 is maintained.

The claims are drawn to a method of inducing an immune response against an infection caused by bacteria from a *Neisseria meningitidis* or *Neisseria gonorrhoeae* in a human in need thereof comprising administering to the human an effective amount of a recombinant protein comprising an amino acid sequence set forth in SEQ ID NO: 4.

Fraser teaches a method of treating an infection due to *Neisseria* bacteria (p. 7 4th full paragraph) in a human (p. 34 2nd full paragraph) by administering to said human an effective amount (p. 36 2nd full paragraph) of immunogenic compositions comprising a protein comprising an amino acid sequence that is 100% identical to SEQ ID NO: 4, thus inducing an immune response to said *Neisseria* bacteria (See p. 32 last paragraph, p. 34 under vaccines). See sequence alignment (provided in previous office action dated 10/31/07) and SEQ ID NO: 1522 on p. 798 of Fraser et al.

Fraser et al teaches said method wherein the bacteria are *Neisseria meningitidis* and wherein the bacteria are *Neisseria gonorrhoeae*. Fraser et al teaches said method comprising administering pharmaceutical compositions of said protein and a pharmaceutically acceptable carrier (p. 34 see under vaccines) wherein said pharmaceutical composition further comprises a polysaccharide antigen (p. 33 4th full paragraph); wherein said composition further comprises inactivated virus particles (inactivated microorganism, p. 33 4th full paragraph); wherein in said pharmaceutical composition further comprises a peptide antigen (p. 35 last paragraph); wherein in said pharmaceutical composition further comprises macrophage colony stimulating factor (growth factor, p. 35 2nd full paragraph); wherein said pharmaceutical composition is administered parenterally (p. 36 2nd to the last paragraph) and wherein said pharmaceutical composition is administered mucosally (via oral route, p. 36 2nd to the last paragraph).

Applicants' arguments:

Applicants respectfully disagree. "In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention 'not novel' or 'anticipated' within section 102, the stated test is whether a reference contains an 'enabling disclosure'...." (citations omitted). "The disclosure in an assertedly anticipating reference must provide an enabling disclosure of the desired subject matter; mere naming or description of the subject matter is insufficient, if it cannot be produced without undue experimentation." MPEP § 2121.01

The Fraser reference fails to be an anticipatory reference because it is not an enabling disclosure. The Fraser reference merely discloses and claims over 3000 sequences that were identified through computer analysis (see, for example, pages 52-53 of Fraser). One skilled in the art would not be able to extrapolate which of the over 3000 disclosed sequences identified through computer analysis would have yielded a predictable immunological properties *in vivo*. The reference fails to provide a specific description as well as enablement of the subject matter of the claims at issue. More specifically, the Fraser reference fails to teach which sequence or fragment is of predictable relevance for a method of inducing an immune response against a N. *meningitidis* or N. *gonorrhoeae* infection in a human in need thereof:

The discover), of which method and what sequence or fragment is required to arrive at the claimed invention would have been sufficiently arduous for one skilled in the art in view the Fraser reference and its over 3000 disclosed sequences. The reference fails to clearly and unequivocally disclose the claimed invention and fails to direct those skilled in the art to the invention without any need for picking or choosing from the vast number of sequences. Fraser does not provide sufficient guidance. Absent such guidance, undue experimentation would be required. As the *MPEP 2121.01* states, "mere naming or description of the subject matter is insufficient, if it cannot be produced without undue experimentation."

Applicants' arguments have been carefully considered but are not found persuasive. Fraser et al is an enabling disclosure. MPEP 2121 states that: When the reference relied on expressly anticipates or makes obvious all of the element of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide *facts* rebutting the presumption of operability. *In re Sasse,* 629 F.2d 675, 207 USPQ 107 (CCPA 1980). MPEP 2121.02 states that: Therefore, applicant must provide evidence showing that a

process for making was not known at the time of the invention. In the instant case, Fraser et al discloses the instant recombinant protein comprising an amino acid sequence set forth in SEQ ID NO: 4 and teaches methods of inducing an immune response against *Neisseria meningitidis* and *Neisseria gonorrhoeae* as set forth above. Fraser et al teaches how to make the protein in expression systems (see p. 9-29) including how to isolate the DNA from *Neisseria* and teaches the DNA sequence encoding the protein (see p.798 SEQ ID NO: 1521 and SEQ ID NO: 1522), teaches how to make pharmaceutical compositions, how to determine therapeutically effective amounts and delivery methods (see p. 33-47). Applicants arguments does not replace an evidentiary showing that attempts to make and use the instant invention were unsuccessful before the date of invention to show inoperability of Fraser et al.

> MPEP 2121.02 (II) states:
>
> When a prior art reference merely discloses the structure of the claimed compound, evidence showing that attempts to prepare that compound were unsuccessful before the date of invention will be adequate to show inoperability. *In re Wiggins*, 488 F.2d 538, 179 USPQ 421 (CCPA 1971). However, the fact that an author of a publication did not attempt to make the compound disclosed, without more, will not overcome a rejection based on that publication. *In re Donohue*, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985) (In this case, the examiner had made a rejection under 35 U.S.C. 102(b) over a publication, which disclosed the claimed compound, in combination with two patents teaching a general process of making the particular class of compounds. The applicant submitted an affidavit stating that the authors of the publication had not actually synthesized the compound. The court held that the fact that the publication's author did not synthesize the disclosed compound was immaterial to the question of reference operability. The patents were evidence that synthesis methods were well known.

Furthermore, as to Applicants argument that one skilled in the art would not be able to extrapolate which of the over 3000 disclosed sequences identified through computer analysis would have yielded a predictable immunological properties *in vivo* and the Fraser reference fails to teach which sequence or fragment is of predictable relevance for a method of inducing an

immune response against a *N. meningitidis* or *N. gonorrhoeae* infection in a human in need thereof is unpersuasive because, *proof of efficacy is not required for a prior art reference to be enabling for purposes of anticipation*

MPEP § 2121 (IIII) states:

> a prior art reference provides an enabling disclosure and thus anticipates a claimed invention if the reference describes the claimed invention in sufficient detail to enable a person of ordinary skill in the art to carry out the claimed invention; *"proof of efficacy is not required for a prior art reference to be enabling for purposes of anticipation."* *Impax Labs. Inc. v. Aventis Pharm. Inc.*, 468 F.3d 1366, 1383, 81 USPQ2d 1001, 1013 (Fed. Cir. 2006). See also MPEP § 2122.

The argument that Fraser et al fails to clearly and unequivocally disclose the claimed invention and fails to direct those skilled in the art to the invention without any need for picking or choosing from the vast number of sequences and fails to provide guidance and that undue experimentation would be required is unpersuasive because Fraser et al discloses that any of the proteins can be used in the manufacture of medicaments for treating and preventing infection due to Neisserial bacteria including *N. meningitidis* and *N. gonorrhoeae* (see above and sequence alignment) and because the instant method using a protein comprising an amino acid sequence set forth in SEQ ID NO: 4 is clearly named by Fraser et al, the disclosure of the protein and its method of use is anticipated no matter how many other species are additionally named.

See MPEP2131.02:

> A REFERENCE THAT CLEARLY NAMES THE CLAIMED SPECIES ANTICIPATES THE CLAIM NO MATTER HOW MANY OTHER SPECIES ARE NAMED
>
> A genus does not always anticipate a claim to a species within the genus. However, when the species is clearly named, the species claim is anticipated no matter how many other species are additionally named. *Ex parte A*, 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990) (The claimed compound was named in a reference which also disclosed 45 other compounds. The Board held that the comprehensiveness of the listing did not negate the

fact that the compound claimed was specifically taught. The Board compared the facts to the situation in which the compound was found in the Merck Index, saying that "the tenth edition of the Merck Index lists ten thousand compounds. In our view, each and every one of those compounds is described' as that term is used in 35 U.S.C. § 102(a), in that publication.").

Thus, in view of the above considerations, the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 32, 35, 36-38, 40, 43-45 and new claim 48 are rejected under 35 U.S.C. 103 as being unpatentable over Fraser et al. WO 99/57280, November 1999 in view of Tai et al (WO 97/28273) Aug. 1997.

The claims are drawn to a method of inducing an immune response against an infection caused by bacteria from a Neisseria meningitidis or *Neisseria gonorrhoeae* in a human in need thereof comprising administering to the human an effective amount of a recombinant protein comprising an amino acid sequence set forth in SEQ ID NO: 4.

Fraser teaches a method of treating an infection due to *Neisseria* bacteria such (p. 7 4th full paragraph) in a human (p. 34 2nd full paragraph) by administering to said human an effective amount (p. 36 2nd full paragraph) of immunogenic compositions comprising a protein comprising an amino acid sequence that is 100% identical to SEQ ID NO: 4, thus inducing an immune response to said *Neisseria* bacteria (see p. 32 last paragraph, p. 34 under vaccines). See sequence alignment (provided in previous office action dated 10/31/07) and SEQ ID NO: 1522 on p. 798 of Fraser et al.

Fraser et al teaches said method wherein the bacteria are *Neisseria meningitidis* and wherein the bacteria are *Neisseria gonorrhoeae*. Fraser et al teaches said method comprising administering pharmaceutical compositions of said protein and a pharmaceutically acceptable carrier (p. 34 see under vaccines) wherein said pharmaceutical composition further comprises a

polysaccharide antigen (p. 33 4th full paragraph); wherein said composition further comprises inactivated virus particles (inactivated microorganism, p. 33 4th full paragraph); wherein in said pharmaceutical composition further comprises a peptide antigen (p. 35 last paragraph); wherein in said pharmaceutical composition further comprises macrophage colony stimulating factor (growth factor, p. 35 2nd full paragraph); wherein said pharmaceutical composition is administered parenterally (p. 36 2nd to the last paragraph) and wherein said pharmaceutical composition is administered mucosally (via oral route, p. 36 2nd to the last paragraph).

Fraser et al does not teach that the polysaccharide antigen is a capsular polysaccharide of *N. meningitidis* and does not teach that said pharmaceutical composition further comprises a bacterial polysaccharide-protein conjugate wherein said protein comprises an amino acid sequence set forth in SEQ ID NO: 4.

Tai et al teaches the use of a composition comprising *N. meningitidis* polysaccharide-*N. meningitidis* protein conjugate to induce an immune response against *Neisseria meningitidis* (See *N. meningitidis* group B polysaccharide conjugated to PorB protein of group B *meningitidis,* p. 32 lines 15-25). Tai et al teach that the T-cell independent quality of polysaccharide antigens in infants can be overcome by conjugating the polysaccharide to a protein carrier (p. 9 lines 8-10). Tai et al teaches the use of *N. meningitidis* proteins as carriers.

It would have been prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to conjugate the protein of Fraser et al to a *N. meningitidis* capsular polysaccharide because Tai et al teaches the use of *N. meningitidis* proteins as carriers in order to overcome the T cell independent quality of polysaccharide antigens in infants.

As to claim 38, it would be prima facie obvious to one of ordinary skill in the art at the time the instant invention was made to combine said composition of Fraser et al and said protein- polysaccharide conjugate because both compositions are used for inducing an immune response against *N. meningitidis* infection. It is prima facie obvious to combine two (or more) compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Applicants' arguments:

Applicants respectfully disagree. The lack of an enabling disclosure in Fraser (as discussed above) and the unpredictable *in vivo* properties of proteins weigh in favor of nonobviousness. The cited references, individually and in combination, fail to provide reasonable prediction of which sequence out of the 3000 computer generated sequences would exhibit the *in vivo* properties to arrive at the claimed invention. The Tai reference fails to compensate for the deficiencies of the Fraser reference. Only with hindsight knowledge can it be argued that it would have been obvious to select and use a recombinant protein comprising an amino acid sequence set forth in SEQ ID NO: 4 having properties for use in a method of inducing an immune response against an infection caused by *N. meningitidis* or *N. gonorrhoeae* in a human in need thereof. The application of hindsight is inappropriate where the prior art does not suggest that this protein could be reasonably expected to manifest the properties and advantages for use in the claimed invention.

Applicants' arguments have been carefully considered but are not persuasive. As to Applicants arguments over the Fraser reference, they have been addressed in detail above. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed

invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Thus, in view of the above considerations, the rejection is maintained.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32, 35-38, 40, 43-45 and 48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of inducing an immune response against an infection caused by bacteria from a *Neisseria meningitidis* or *Neisseria gonorrhoeae* in a human in need thereof comprising administering to the human an effective amount of a recombinant protein comprising *an* amino acid sequence set forth in SEQ ID NO: 4.

The scope of the claims includes methods of inducing an immune response using a recombinant protein comprising fragments of SEQ ID NO: 4 (i.e. because the recombinant

protein comprising *an* amino acid sequence set forth in SEQ ID NO: 4) or comprising SEQ ID NO: 4.

The specification teaches that SEQ ID NO: 4 induces an immune response when administered to mice (p. 17 example 6). The specification also teaches that immune sera obtained from said immunized mice reduced bacterial counts in rats challenged with bacteria (strain CU385) one hour after administering said sera (p.17 example 7, and see figure 10). The specification does not reduce to practice a method of inducing an immune response against an infection caused by bacteria from a *Neisseria meningitidis* or *Neisseria gonorrhoeae* comprising administering a recombinant protein comprising any fragment of SEQ ID NO: 4 (a recombinant protein comprising *an* amino acid sequence set forth in SEQ ID NO: 4).

The recitation of "a recombinant protein comprising *an* amino acid sequence set forth in SEQ ID NO: 4" indicates fragments i.e. any amino acid sequence set forth in SEQ ID NO: 4 is included in the scope of the invention. This is drawn to a genus of fragments comprising numerous species of varying lengths and varying sequence structure. The specification only provides description of a recombinant protein comprising *the* amino acid sequence set forth in SEQ ID NO: 4 that induces an immune response. The specification does not describe the immunogenic fragments of SEQ ID NO: 4 or the common structure of the genus of fragments of SEQ ID NO: 4 that is immunogenic. The specification does not teach the immunogenic epitope(s) of SEQ ID NO: 4.

Antibody epitopes are characterized by the art as either continuous or discontinuous (see pages 23-25, 27-33, Harlow et al , Antibodies A Laboratory Manual, Cold Spring Harbor Laboratory Press Inc., 1988). T cell epitopes are continuous peptide fragments of a polypeptide

or antigen that have been processed by an accessory cell. The art recognizes that defining epitopes is not easy and there is a confusing divergence between the textbook definition of epitope and the definition that is in use in published descriptions of experimental investigations and that epitopes must be empirically determined (Greenspan et al, Nature Biotechnology 17:936-937, 1999). The specification clearly lacks description of any particular antibody epitope (i.e. antigenic determinant), either continuous or discontinuous that is within SEQ ID NO: 4 or T cell epitope. These particular characteristics of the B or T cell epitope is required by the for the skilled artisan to envision the common structural elements of the genus of fragment required to practice the claimed invention that is able to induce an immune response against *Neisseria meningitidis* or *Neisseria gonorrhoeae.*

For example, Colman et al. (Research in Immunology 145: 33-36, 1994, p.33 column 2, p. 35 column 1) disclose that a single amino acid changes in an antigen can effectively abolish the interaction with an antibody entirely and that a very conservative amino acid substitution may abolish antibody binding and a non-conservative amino substitution may have little effect in antibody binding. This underlies the importance of the description of the immunoepitopes that induces an immune response to *Neisseria meningitidis* or *Neisseria gonorrhoeae* and where and how many changes can the immunoepitopes tolerate and still retain the ability to induce an immune response to *Neisseria meningitidis* or *Neisseria gonorrhoeae.* Houghten et al. (New Approaches to Immunization, Vaccines 86, Cold Spring Harbor Laboratory, p. 21-25, 1986) taught the criticality of individual amino acid residues and their positions in peptide antigen-antibody interactions. Houghten et al state (see page 24): "One could expect point mutations in the protein antigen to cause varying degrees of loss of protection (in the instant case the ability to

induce an immune response against *Neisseria meningitidis* or *Neisseria gonorrhoeae*), depending on the relative importance of the binding interaction of the altered residue. A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations [including deletions to obtain fragments] at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies in the polyclonal pool."

The fact that one could screen for immunoepitopes that is able to induce an immune response to *Neisseria meningitidis* or *Neisseria gonorrhoeae* is not the standard for written description. Even though one could screen for which changes in SEQ ID NO: 4 or which fragments will maintain the ability to induce an immune response against *Neisseria meningitidis* or *Neisseria gonorrhoeae*, the courts have held that possession of a genus may not be shown by merely describing how to obtain members of the claimed genus or how to identify their common structural features. The written description requirement is separate and distinct from the enablement requirement (See also *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 920-23, 69 USPQ2d 1886, 1890-93 (Fed. Cir. 2004) and adequate written description requires more than a mere reference to a potential method for identifying candidate polypeptides. The purpose of the written description requirement is broader than to merely explain how to 'make and use' [the invention] *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1560, 19 USPQ2d 1111, 1114 (Fed. Cir. 1991). The disclosure of only one member of the large and widely variant genus to which the claims are drawn is insufficient to describe the large and variant genus of fragments the scope of which is set forth above. In such an unpredictable art, as set forth supra (i.e. defining immunoepitopes), adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. See *Noelle v*

Lederman. 355 F. 3d 1343, 1350, 69 USPQ2d 1508, 1514 (*Fed. Cir. 2004*) and *In re Alonso* (Fed. Cir. 2008-1079).

Since the specification does not describe the common structure i.e. the immunoepitope(s) capable of inducing an immune response against *Neisseria meningitidis* or *Neisseria gonorrhoeae*, the skilled artisan would not be able to readily envision which fragments of SEQ ID NO: 4 maintain the capability of inducing an immune response to a *Neisseria meningitidis* or *Neisseria gonorrhoeae* as compared to the full sequence. Except for SEQ ID NO:4 i.e. the specification lacks written description for the instantly claimed method of inducing an immune response using a recombinant protein comprising *an* amino acid sequence set forth in SEQ ID NO: 4 (i.e. fragments)and Applicants as of the time of filing were not in possession of said method. However, Applicants were in possession of a method of inducing an immune response against an infection caused by bacteria from a *Neisseria meningitidis* or *Neisseria gonorrhoeae* in a human in need thereof comprising administering to the human an effective amount of a recombinant protein comprising *the* amino acid sequence set forth in SEQ ID NO: 4.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 47 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A method of inducing an immune response against an infection caused by *Neisseria meningitidis* or *Neisseria gonorrhoeae* bacteria in a human in need thereof, comprising administering to the human an effective amount of a recombinant protein encoded by an amino acid sequence consisting of SEQ ID NO: 4.

Amino acid sequences do not 'code' for proteins. A protein comprises an amino acid sequence. A nucleic acid sequences comprises a genetic code which 'codes' or 'encodes' a protein. A code for an amino acid sequence is a codon and consists of a sequence of three nucleotide base pairs (triplet codon). Thus, an amino acid sequence does not encode a protein is as an amino acid sequence does not contain a genetic code or a sequence of triplet codons.

Status of Claims

Claims 32, 35-38, 40, 43-45 and 47-48 are rejected. No claims allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Oluwatosin Ogunbiyi whose telephone number is 571-272-9939. The examiner can generally be reached on M-F 8:30 am - 5:00 pm. If attempts to reach the

examiner by telephone are unsuccessful, the examiner's supervisor Robert Mondesi can be reached at 571-272-0956.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Oluwatosin Ogunbiyi/
Examiner, Art Unit 1645
/Robert B Mondesi/
Supervisory Patent Examiner, Art Unit 1645